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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/939,483	08/24/2001	Fabrice Duprat	1201-CIP-DIV-2-00	3851

35811 7590 03/08/2005

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EXAMINER

BERTOGLIO, VALARIE E

ART UNIT PAPER NUMBER

1632

DATE MAILED: 03/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/939,483

Applicant(s)

DUPRAT ET AL.

Examiner

Valarie Bertoglio

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 07 February 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 32 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 32 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 24 August 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

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### **DETAILED ACTION**

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 02/07/2005 has been entered.

#### ***Priority***

The amendment updating the status of the priority documents was located in the transmittal sheet accompanying the application. The priority information is now correct.

#### ***Specification***

The disclosure is objected to because of the following informalities: The transmittal sheet accompanying the application submitted that updated priority information should be inserted before the previous priority statement. The previous statement is present as the second sentence of the specification and should be removed.

Appropriate correction is required.

#### ***Sequence Compliance***

The application is now sequence compliant.

#### ***Claim Rejections - 35 USC § 112-1<sup>st</sup> paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claim 32 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.'" (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

1) The aspect of the previous rejection relating to the lack of phenotype of the claimed mouse is maintained (see pages 4-5, specifically paragraph bridging pages 4-5 of the previous office action).

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Applicant has argued that a claim is enabled when the specification teaches one skilled in the art how to make and use the claimed invention without undue experimentation. Applicant argues that there is no recitation of a phenotype in the claim that requires that the knockout mouse have a certain phenotype other than it be deficient in expression of TASK. Applicant further argues that concerns relating to the phenotype of the claimed mouse are misplaced because no phenotype is required as the claims do not include or require such limitations. Applicant cites *Exparte Chen* in arguing that despite the Examiner setting forth the unpredictability of phenotype in transgene knock-in animals, the board considered claims drawn to transgenic carp without a phenotypic limitation, to be enabled, *Exparte Chen* 61 USPQ2d 1026 (BPAI 2001, unpublished).

In response, without a phenotype, either in the claim or in the specification, the skilled artisan will not know how to use the claimed mouse because it fails to differ from any wild-type mouse. With respect to *Chen*, the court addressed an enablement rejection that was based on the low reproducibility and low frequency of success inherent in the nature of making transgenic fish. The board determined that extreme repetition to obtain the claimed product does not constitute undue experimentation. The board was not addressing the phenotypic limitations or lack thereof in the claims. Finally, the requirement is not to add a phenotypic limitation to the claim. The instant rejection, which is based on an entirely different issue of enablement in comparison to the issue with *Chen* concerning use of the claimed product, results from the lack of the specification to provide an enabled use. No phenotype is taught, or claimed, for the mouse. The specification contains only prophetic teachings regarding making the claimed transgenic mouse (page 28, lines 12-18). Without guidance regarding a phenotype, undue experimentation

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would be required by the skilled artisan to determine how to use the claimed mice. In light of the unpredictability of phenotype in the art, the skilled artisan cannot predict, based on the guidance provided in the specification what the phenotype of the claimed mouse would be and therefore, the skilled artisan would not know how to use the mouse. It is noted that *Exparte Chen* is an unpublished opinion.

As set forth in the previous office action, the specification is required to provide an enabling disclosure for the claimed mouse. The requirement includes an enabling disclosure for both making and using the claimed mouse. The specification fails to describe any phenotypic characteristics of the claimed mouse that would allow the skilled artisan to know how to use the mouse and claim 32 does not recite a phenotypic limitation for the claimed mouse such that the skilled artisan would readily know how to use the claimed mouse. As set forth in the previous office action, the phenotype of knockout mice is unpredictable. In vitro characterization of the function of the human TASK protein (pages 19-23) as disclosed in the specification is not sufficient to overcome the unpredictability of phenotype known in the art such that the skilled artisan would know how to use the claimed mouse.

2) The specification is not enabling for the full breadth of the genus of genes knocked out as encompassed by the claim as written. Claim 32 is broad in that it encompasses knockout of any gene in a mouse that results in the loss of the expression of the gene product set forth by SEQ ID NO:5.

The specification teaches the cloning of a partial cDNA encoding a potassium transport channel called TASK. The partial amino acid sequence of TASK, lacking the N-terminal amino acids, is set forth by SEQ ID NO:5 (pages 16-17). The specification contemplates generating

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transgenic animals that either supra-express a protein of the TASK family of potassium channels or a knock-out animal having a deficiency for said channels (page 28, lines 12-18). The specification does not teach how to make the claimed mice, does not teach what nucleic acid sequences to use to make the claimed mice and does not teach a phenotypic effect of the gene disruption.

The claims broadly encompass knocking out any gene that indirectly causes a deficiency in the expression of the potassium transport channel comprising SEQ ID NO:5. The specification does not provide any guidance with respect to what genes might alter production of the claimed gene product when disrupted themselves. The skilled artisan would not know what genes to knockout to cause the claimed deficiency other than a gene encoding the gene product.

It is noted that SEQ ID NO:5 is not a complete polypeptide sequence (see page 17, lines 10-13). Thus, SEQ ID NO:5 does not represent a polypeptide that is normally expressed in mice. Therefore, there would be no corresponding genomic locus encoding SEQ ID NO:5 and the skilled artisan would not know how to find or disrupt a genomic locus encoding the claimed non-existing protein.

3) Claim 32, as written also encompasses chimeric mice (genetic mosaics) wherein only a portion of the cells of the mouse comprises the claimed genetic disruption. The specification fails to enable using chimeric mice because no useful phenotype is taught by the instant specification for the chimeric mice. Inherent in the art of making genetic mosaic animals is the unpredictability of how many and which cells will comprise a genetic alteration. The specification does not provide guidance on the production of a chimeric mouse comprising a genomic disruption resulting in the deficiency of the potassium ion channel set forth by SEQ ID

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NO:5, where only some portion of the mouse's cells have the disruption. It is not predictable what the phenotype of each of the chimeras possessing a different proportion of cells comprising the gene disruption would be. At the time of filing it would have been required of the skilled artisan to perform an undue amount of experimentation without a predictable degree of success how to make and use the chimeric mice encompassed by the claims. Applicant should overcome this aspect of the rejection by adopting claim language such as "a transgenic mouse whose genome comprises a disruption".

Therefore, in light of the lack of guidance with respect to how to use the claimed mod the breadth of the claims with respect to the gene disrupted in the mouse and with respect to chimeric mice, it would require undue experimentation for one of ordinary skill in the art to determine how to make and use the invention as broadly claimed.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The previous rejection of claim 32 under 35 USC 112, second paragraph, is withdrawn in light of Applicant's amendment to the claim.



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***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725.

The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Valarie Bertoglio

Examiner

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